

### **Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application;

### **Listing of Claims:**

Claims 1-149 were previously cancelled.

Claims 150-187 are currently cancelled.

New Claims 188-246 are currently added.

188. (New) A method of identifying an agent that ameliorates or modulates a phenotype or neurological disorder; cardiovascular, endothelial or angiogenic disorder; eye abnormality; immunological disorder; oncological disorder; bone metabolic abnormality or disorder; lipid metabolic disorder; or developmental abnormality, associated with a disruption in a gene which encodes a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide, the method comprising:

- (a) providing a non-human transgenic animal whose genome comprises a disruption of a gene which is an ortholog of a human gene that encodes a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide;
- (b) measuring a physiological characteristic of the non-human transgenic animal of (a);
- (c) comparing the measured physiological characteristic of (b) with that of a gender matched wild-type animal, wherein the physiological characteristic of the non-human transgenic animal that differs from the physiological characteristic of the gender matched wild-type animal is identified as a phenotype or disorder resulting from the gene disruption in the non-human transgenic animal;
- (d) administering a test agent to said non-human transgenic animal; and
- (e) determining whether said test agent ameliorates or modulates the phenotype or neurological disorder; cardiovascular, endothelial or angiogenic disorder; eye abnormality;

immunological disorder; oncological disorder; bone metabolic abnormality or disorder; lipid metabolic disorder; or developmental abnormality in the non-human transgenic animal.

189. (New) The method of Claim 188, wherein the neurological disorder is an increased anxiety-like response during open field activity testing.

190. (New) The method of Claim 188, wherein the neurological disorder is a decreased anxiety-like response during open field activity testing.

191. (New) The method of Claim 188, wherein the neurological disorder is depression, generalized anxiety disorder, attention deficit disorder, sleep disorder, hyperactivity disorder, obsessive compulsive disorder, schizophrenia, cognitive disorder, hyperalgesia or sensory disorder.

192. (New) The method of Claim 188, wherein the eye abnormality is a retinal abnormality.

193. (New) The method of Claim 188, wherein the eye abnormality is consistent with vision problems or blindness.

194. (New) The method of Claim 188, wherein the eye abnormality is consistent with retinal degeneration or retinal dysplasia, various retinopathies, including retinopathy of prematurity, retrolental fibroplasia, neovascular glaucoma, age-related macular degeneration, diabetic macular edema, corneal neovascularization, corneal graft neovascularization, corneal graft rejection, retinal/choroidal neovascularization, neovascularization of the angle (rubeosis), ocular neovascular disease, vascular restenosis, arteriovenous malformations (AVM), meningioma, hemangioma, angiofibroma, thyroid hyperplasias (including Grave's disease), corneal and other tissue transplantation, retinal artery obstruction or occlusion; retinal degeneration causing secondary atrophy of the retinal vasculature, retinitis pigmentosa, macular dystrophies, Stargardt's disease, congenital stationary night blindness, choroideremia, gyrate atrophy, Leber's

congenital amaurosis, retinoschisis disorders, Wagner's syndrome, Usher syndromes, Zellweger syndrome, Saldino-Mainzer syndrome, Senior-Loken syndrome, Bardet-Biedl syndrome, Alport's syndrome, Alstrom's syndrome, Cockayne's syndrome, dysplasia spondyloepiphysearia congenita, Flynn-Aird syndrome, Friedreich ataxia, Hallgren syndrome, Marshall syndrome, Albers-Schnoberg disease, Refsum's disease, Kearns-Sayre syndrome, Waardenburg's syndrome, Alagille syndrome, myotonic dystrophy, olivopontocerebellar atrophy, Pierre-Marie syndrome, Stickler syndrome, carotidemia, cystinosis, Wolfram syndrome, Bassen-Kornzweig syndrome, abetalipoproteinemia, incontinentia pigmenti, Batten's disease, mucopolysaccharidoses, homocystinuria, or mannosidosis.

195. (New) The method of Claim 188, wherein the eye abnormality is a cataract.

196. (New) The method of Claim 195, wherein the cataract is consistent with systemic diseases such as human Down's syndrome, Hallerman-Streiff syndrome, Lowe syndrome, galactosemia, Marfan syndrome, Trismoy 13-15, Alport syndrome, myotonic dystrophy, Fabry disease, hypoparathyroidism or Conradi syndrome.

197. (New) The method of Claim 188, wherein the developmental abnormality comprises embryonic lethality or reduced viability.

198. (New) The method of Claim 188, wherein the cardiovascular, endothelial or angiogenic disorder is consistent with arterial diseases, such as diabetes mellitus; papilledema; optic atrophy; atherosclerosis; angina; myocardial infarctions such as acute myocardial infarctions, cardiac hypertrophy, and heart failure such as congestive heart failure; hypertension; inflammatory vasculitides; Reynaud's disease and Reynaud's phenomenon; aneurysms and arterial restenosis; venous and lymphatic disorders such as thrombophlebitis, lymphangitis, and lymphedema; peripheral vascular disease; cancer such as vascular tumors, e.g., hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, Kaposi's sarcoma,

lymphangioma, and lymphangiosarcoma; tumor angiogenesis; trauma such as wounds, burns, and other injured tissue, implant fixation, scarring; ischemia reperfusion injury; rheumatoid arthritis; cerebrovascular disease; renal diseases such as acute renal failure, or osteoporosis.

199. (New) The method of Claim 188, wherein the immunological disorder is consistent with systemic lupus erythematosus; rheumatoid arthritis; juvenile chronic arthritis spondyloarthropathies; systemic sclerosis (scleroderma); idiopathic inflammatory myopathies (dermatomyositis, polymyositis); Sjögren's syndrome; systemic vasculitis; sarcoidosis; autoimmune hemolytic anemia (immune pancytopenia, paroxysmal nocturnal hemoglobinuria); autoimmune thrombocytopenia (idiopathic thrombocytopenic purpura, immune-mediated thrombocytopenia); thyroiditis (Grave's disease, Hashimoto's thyroiditis, juvenile lymphocytic thyroiditis, atrophic thyroiditis); diabetes mellitus; immune-mediated renal disease (glomerulonephritis, tubulointerstitial nephritis); demyelinating diseases of the central and peripheral nervous systems such as multiple sclerosis, idiopathic demyelinating polyneuropathy or Guillain-Barré syndrome, and chronic inflammatory demyelinating polyneuropathy; hepatobiliary diseases such as infectious hepatitis (hepatitis A, B, C, D, E and other non-hepatotropic viruses), autoimmune chronic active hepatitis, primary biliary cirrhosis, granulomatous hepatitis, and sclerosing cholangitis; inflammatory bowel disease (ulcerative colitis: Crohn's disease); gluten-sensitive enteropathy, and Whipple's disease; autoimmune or immune-mediated skin diseases including bullous skin diseases, erythema multiforme and contact dermatitis, psoriasis; allergic diseases such as asthma, allergic rhinitis, atopic dermatitis, food hypersensitivity and urticaria; immunologic diseases of the lung such as eosinophilic pneumonia, idiopathic pulmonary fibrosis and hypersensitivity pneumonitis; or transplantation-associated diseases including graft rejection and graft -versus-host disease.

200. (New) The method of Claim 188, wherein said bone metabolic abnormality or disorder is arthritis, osteoporosis or osteopetrosis.

201. (New) The method of Claim 188, wherein the non-human transgenic animal exhibits at least one of the following physiological characteristics compared with gender matched wild-type littermates: a decreased anxiety-like response during open field activity testing; an increased anxiety-like response during open field activity testing; balding, exothalamus observations, and piloerection observations in functional observation battery (FOB) testing; an increased mean artery-to-vein ratio associated with retinal degeneration; developing cataracts; an increased mean serum cholesterol level; an increased mean serum triglyceride level; a decreased mean serum insulin level, a decreased mean percentage of B cells in the spleen and lymph node; a decreased mean serum IgG2a response to an ovalbumin challenge; decreased mean serum IgA levels; an increased mean serum IgG2a response to an ovalbumin challenge; increased mean serum IgM, IgG1, IgG2a and IgG2b levels; increased mean serum IgM, IgA and IgG3 levels; increased mean serum IgM, IgG1, IgG2a and IgG2b levels; an increased mean percentage of CD4 cells and a decreased mean percentage of CD8 cells in spleen and thymus; mobilization of neutrophils in response to peritoneal inflammation; an enhanced DDS-induced colitis response; an enhanced ConA-induced hepatitis response; a decreased skin fibroblast proliferation; a decreased volumetric bone mineral density, a decreased bone mineral content index (BMC/LBM), and a decreased mean bone mineral density in total body, femur and vertebrae; a decreased mean bone mineral density, a decreased mean trabecular bone volume, decreased thickness, and decreased connectivity density; a decreased body weight and length, decreased total tissue mass and lean body mass, a decreased femoral midshaft cross-sectional area with decreased alkaline phosphatase levels; growth retardation with decreased body weight and length, total tissue mass, and lean body mass; a diaphragmatic hernia; an increased total tissue mass, increased lean body mass, increased bone mineral content, increased total body and increased femoral bone mineral density; an enhanced glucose tolerance; developmental disorders including abnormal kidney development marked by kidney agenesis; embryonic lethality; or embryonic lethality wherein heterozygous adults exhibited decreased serum IgM, IgG1, IgG2a, IgG2b and IgG3 levels.

202. (New) An agent identified by the method of Claim 188.

203. (New) The agent of Claim 202 which is an agonist or antagonist of a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide.

204. (New) The agent of Claim 203, wherein the agonist is an anti-PRO224, anti-PRO9783, anti-PRO1108, anti-PRO34000, anti-PRO240, anti-PRO943, anti-hu A33, anti-PRO230, anti-PRO178, anti-PRO1199, anti-PRO4333, anti-PRO1336, anti-PRO19598, anti-PRO1083, anti-hu TRPM2 or anti-PRO1801 antibody.

205. (New) The agent of Claim 203, wherein the antagonist is an anti-PRO224, anti-PRO9783, anti-PRO1108, anti-PRO34000, anti-PRO240, anti-PRO943, anti-hu A33, anti-PRO230, anti-PRO178, anti-PRO1199, anti-PRO4333, anti-PRO1336, anti-PRO19598, anti-PRO1083, anti-hu TRPM2 or anti-PRO1801 antibody.

206. (New) A method of ameliorating or modulating a phenotype or neurological disorder; cardiovascular, endothelial or angiogenic disorder; eye abnormality; immunological disorder; oncological disorder; bone metabolic abnormality or disorder; lipid metabolic disorder; or developmental abnormality associated with a gene that encodes a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide, the method comprising administering to a subject whom may already have the phenotype or disorder, or may be prone to have the phenotype or disorder, or may be in whom the phenotype or disorder is to be prevented, an effective amount of the agent of Claim 202, or agonist or antagonist of a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide, thereby effectively ameliorating or modulating the phenotype or disorder.

207. (New) A method of evaluating a therapeutic agent capable of affecting a condition or neurological disorder; cardiovascular, endothelial or angiogenic disorder; eye abnormality;

immunological disorder; oncological disorder; bone metabolic abnormality or disorder; lipid metabolic disorder; or developmental abnormality, associated with a disruption in a gene which encodes a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide, the method comprising:

- (a) providing a non-human transgenic animal whose genome comprises a disruption of a gene which is an ortholog of a human gene that encodes a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide;
- (b) measuring a physiological characteristic of the non-human transgenic animal of (a);
- (c) comparing the measured physiological characteristic of (b) with that of a gender matched wild-type animal, wherein the physiological characteristic of the non-human transgenic animal that differs from the physiological characteristic of the gender matched wild-type animal is identified as a condition resulting from the gene disruption in the non-human transgenic animal;
- (d) administering a test agent to the non-human transgenic animal of (a); and
- (e) evaluating the effects of the test agent on the identified condition or disorder associated with gene disruption in the non-human transgenic animal.

208. (New) A therapeutic agent identified by the method of Claim 207.

209. (New) The therapeutic agent of Claim 208 which is an agonist or antagonist of a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide.

210. (New) The therapeutic agent of Claim 209, wherein the agonist is an anti-PRO224, anti-PRO9783, anti-PRO1108, anti-PRO34000, anti-PRO240, anti-PRO943, anti-hu A33, anti-PRO230, anti-PRO178, anti-PRO1199, anti-PRO4333, anti-PRO1336, anti-PRO19598, anti-PRO1083, anti-hu TRPM2 or anti-PRO1801 antibody.

211. (New) The therapeutic agent of Claim 209, wherein the antagonist is an anti-PRO224, anti-PRO9783, anti-PRO1108, anti-PRO34000, anti-PRO240, anti-PRO943, anti-hu A33, anti-PRO230, anti-PRO178, anti-PRO1199, anti-PRO4333, anti-PRO1336, anti-PRO19598, anti-PRO1083, anti-hu TRPM2 or anti-PRO1801 antibody.

212. (New) A pharmaceutical composition comprising the therapeutic agent of Claim 208.

213. (New) A method of treating or preventing or ameliorating a condition or neurological disorder; cardiovascular, endothelial or angiogenic disorder; eye abnormality; immunological disorder; oncological disorder; bone metabolic abnormality or disorder, or embryonic lethality associated with a gene that encodes a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide, the method comprising administering to a subject in need of such treatment whom may already have the condition or disorder, or may be prone to have the condition or disorder or may be in whom the condition or disorder is to be prevented, a therapeutically effective amount of the therapeutic agent of Claim 208, or agonist or antagonist of a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide, thereby effectively treating or preventing or ameliorating said condition or disorder.

214. (New) The method of Claim 213, wherein the neurological disorder is an increased anxiety-like response during open field activity testing.

215. (New) The method of Claim 213, wherein the neurological disorder is a decreased anxiety-like response during open field activity testing.

216. (New) The method of Claim 213, wherein the neurological disorder is depression, generalized anxiety disorder, attention deficit disorder, sleep disorder, hyperactivity disorder,



obsessive compulsive disorder, schizophrenia, cognitive disorder, hyperalgesia or sensory disorder.

217. (New) The method of Claim 213, wherein the eye abnormality is a retinal abnormality.

218. (New) The method of Claim 213, wherein the eye abnormality is consistent with vision problems or blindness.

219. (New) The method of Claim 213, wherein the eye abnormality is consistent with retinal degeneration or retinal dysplasia, various retinopathies, including retinopathy of prematurity, retrolental fibroplasia, neovascular glaucoma, age-related macular degeneration, diabetic macular edema, corneal neovascularization, corneal graft neovascularization, corneal graft rejection, retinal/choroidal neovascularization, neovascularization of the angle (rubeosis), ocular neovascular disease, vascular restenosis, arteriovenous malformations (AVM), meningioma, hemangioma, angiofibroma, thyroid hyperplasias (including Grave's disease), corneal and other tissue transplantation, retinal artery obstruction or occlusion; retinal degeneration causing secondary atrophy of the retinal vasculature, retinitis pigmentosa, macular dystrophies, Stargardt's disease, congenital stationary night blindness, choroideremia, gyrate atrophy, Leber's congenital amaurosis, retinoschisis disorders, Wagner's syndrome, Usher syndromes, Zellweger syndrome, Saldino-Mainzer syndrome, Senior-Loken syndrome, Bardet-Biedl syndrome, Alport's syndrome, Alstrom's syndrome, Cockayne's syndrome, dysplasia spondyloepiphysearia congenita, Flynn-Aird syndrome, Friedreich ataxia, Hallgren syndrome, Marshall syndrome, Albers-Schnoberg disease, Refsum's disease, Kearns-Sayre syndrome, Waardenburg's syndrome, Alagille syndrome, myotonic dystrophy, olivopontocerebellar atrophy, Pierre-Marie syndrome, Stickler syndrome, carotinemia, cystinosis, Wolfram syndrome, Bassen-Kornzweig syndrome, abetalipoproteinemia, incontinentia pigmenti, Batten's disease, mucopolysaccharidoses, homocystinuria, or mannosidosis.

220. (New) The method of Claim 213, wherein the eye abnormality is a cataract.

221. (New) The method of Claim 220, wherein the cataract is a systemic disease such as human Down's syndrome, Hallerman-Streiff syndrome, Lowe syndrome, galactosemia, Marfan syndrome, Trismoy 13-15, Alport syndrome, myotonic dystrophy, Fabry disease, hypoparathroidism or Conradi syndrome.

222. (New) The method of Claim 213, wherein the developmental abnormality comprises embryonic lethality or reduced viability.

223. (New) The method of Claim 213, wherein the cardiovascular, endothelial or angiogenic disorder is consistent with arterial diseases, such as diabetes mellitus; papilledema; optic atrophy; atherosclerosis; angina; myocardial infarctions such as acute myocardial infarctions, cardiac hypertrophy, and heart failure such as congestive heart failure; hypertension; inflammatory vasculitides; Reynaud's disease and Reynaud's phenomenon; aneurysms and arterial restenosis; venous and lymphatic disorders such as thrombophlebitis, lymphangitis, and lymphedema; peripheral vascular disease; cancer such as vascular tumors, e.g., hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, Kaposi's sarcoma, lymphangioma, and lymphangiosarcoma; tumor angiogenesis; trauma such as wounds, burns, and other injured tissue, implant fixation, scarring; ischemia reperfusion injury; rheumatoid arthritis; cerebrovascular disease; renal diseases such as acute renal failure, or osteoporosis.

224. (New) The method of Claim 213, wherein the immunological disorder is consistent with systemic lupus erythematosus; rheumatoid arthritis; juvenile chronic arthritis; spondyloarthropathies; systemic sclerosis (scleroderma); idiopathic inflammatory myopathies (dermatomyositis, polymyositis); Sjögren's syndrome; systemic vasculitis; sarcoidosis; autoimmune hemolytic anemia (immune pancytopenia, paroxysmal nocturnal hemoglobinuria); autoimmune thrombocytopenia (idiopathic thrombocytopenic purpura, immune-mediated thrombocytopenia); thyroiditis (Grave's disease, Hashimoto's thyroiditis, juvenile lymphocytic

thyroiditis, atrophic thyroiditis); diabetes mellitus; immune-mediated renal disease (glomerulonephritis, tubulointerstitial nephritis); demyelinating diseases of the central and peripheral nervous systems such as multiple sclerosis, idiopathic demyelinating polyneuropathy or Guillain-Barré syndrome, and chronic inflammatory demyelinating polyneuropathy; hepatobiliary diseases such as infectious hepatitis (hepatitis A, B, C, D, E and other non-hepatotropic viruses), autoimmune chronic active hepatitis, primary biliary cirrhosis, granulomatous hepatitis, and sclerosing cholangitis; inflammatory bowel disease (ulcerative colitis: Crohn's disease); gluten-sensitive enteropathy, and Whipple's disease; autoimmune or immune-mediated skin diseases including bullous skin diseases, erythema multiforme and contact dermatitis, psoriasis; allergic diseases such as asthma, allergic rhinitis, atopic dermatitis, food hypersensitivity and urticaria; immunologic diseases of the lung such as eosinophilic pneumonia, idiopathic pulmonary fibrosis and hypersensitivity pneumonitis; or transplantation associated diseases including graft rejection and graft -versus-host disease.

225. (New) The method of Claim 213, wherein said bone metabolic abnormality or disorder is arthritis, osteoporosis or osteopetrosis.

226. (New) A method of identifying an agent that mimics a condition or phenotype associated with a disruption in a gene which encodes a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide, the method comprising:

(a) providing a non-human transgenic animal whose genome comprises a disruption of a gene which is an ortholog of a human gene that encodes a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide;

(b) measuring a physiological characteristic of the non-human transgenic animal of (a);

(c) comparing the measured physiological characteristic of (b) with that of a gender matched wild-type animal, wherein the physiological characteristic of the non-human transgenic animal that differs from the physiological characteristic of the gender matched wild-type animal

is identified as a condition or phenotype resulting from the gene disruption in the non-human transgenic animal;

- (d) administering a test agent to said gender matched wild-type animal; and
- (e) determining whether said test agent mimics the condition or phenotype initially observed in the non-human transgenic animal.

227. (New) The method of Claim 226, wherein the condition or phenotype associated with the disruption of the gene which is an ortholog of a human gene that encodes a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide is enhanced glucose tolerance.

228. (New) The method of Claim 226, wherein the condition or phenotype associated with the disruption of the gene which is an ortholog of a human gene that encodes a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide is increased insulin sensitivity.

229. (New) An agent identified by the method of Claim 226.

230. (New) The agent of Claim 229 which is an antagonist of a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide.

231. (New) The agent of Claim 230, wherein the antagonist is an anti-PRO224, anti-PRO9783, anti-PRO1108, anti-PRO34000, anti-PRO240, anti-PRO943, anti-hu A33, anti-PRO230, anti-PRO178, anti-PRO1199, anti-PRO4333, anti-PRO1336, anti-PRO19598, anti-PRO1083, anti-hu TRPM2 or anti-PRO1801 antibody.

232. (New) A method of mimicking a condition or phenotype associated with a disruption of a gene which encodes a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide, the method comprising administering to a subject in whom the condition or phenotype is to be mimicked, an effective amount of the agent of Claim 229 or an antagonist of a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide, thereby effectively mimicking the condition or phenotype.

233. (New) The method of Claim 232, wherein the condition or phenotype associated with the disruption of the gene which is an ortholog of a human gene that encodes a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide is enhanced glucose tolerance.

234. (New) The method of Claim 232, wherein the condition or phenotype associated with the disruption of the gene which is an ortholog of a human gene that encodes a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide is increased insulin sensitivity.

235. (New) A method of evaluating a therapeutic agent capable of mimicking a condition or phenotype associated with a disruption of a gene which encodes a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide, the method comprising:

(a) providing a non-human transgenic animal whose genome comprises a disruption of a gene which is an ortholog of a human gene that encodes a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide;

- (b) measuring a physiological characteristic of the non-human transgenic animal of (a);
- (c) comparing the measured physiological characteristic of (b) with that of a gender matched wild-type animal, wherein the physiological characteristic of the non-human transgenic animal that differs from the physiological characteristic of the gender matched wild-type animal is identified as a condition or phenotype resulting from the gene disruption in the non-human transgenic animal;
- (d) administering a test agent to said gender matched wild-type animal of (c); and
- (e) evaluating the ability of the test agent to mimic the condition or phenotype associated with gene disruption in the non-human transgenic animal.

236. (New) A therapeutic agent identified by the method of Claim 235.

237. (New) The therapeutic agent of Claim 236 which is an antagonist of a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide.

238. (New) The therapeutic agent of Claim 237, wherein the antagonist is an anti-PRO224, anti-PRO9783, anti-PRO1108, anti-PRO34000, anti-PRO240, anti-PRO943, anti-hu A33, anti-PRO230, anti-PRO178, anti-PRO1199, anti-PRO4333, anti-PRO1336, anti-PRO19598, anti-PRO1083, anti-hu TRPM2 or anti-PRO1801 antibody.

239. (New) A pharmaceutical composition comprising the therapeutic agent of Claim 236.

240. (New) A method of mimicking a condition or phenotype associated with a disruption of a gene which encodes a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide, the method comprising administering to a subject in whom the condition or phenotype disorder is to be mimicked, a therapeutically effective amount of the therapeutic agent of Claim 236, or an antagonist of a PRO224, PRO9783, PRO1108, PRO34000, PRO240,

PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide, thereby effectively mimicking the condition or phenotype.

241. (New) A method of identifying an agent that modulates the expression of a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide; the method comprising:

(a) contacting a test agent with a host cell expressing a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide; and

(b) determining whether the test agent modulates the expression of the PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide by the host cell.

242. (New) An agent identified by the method of Claim 241.

243. (New) The agent of Claim 242 which is an agonist or antagonist of a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide.

244. (New) The agent of Claim 243, wherein the agonist is an anti-PRO224, anti-PRO9783, anti-PRO1108, anti-PRO34000, anti-PRO240, anti-PRO943, anti-hu A33, anti-PRO230, anti-PRO178, anti-PRO1199, anti-PRO4333, anti-PRO1336, anti-PRO19598, anti-PRO1083, anti-hu TRPM2 or anti-PRO1801 antibody.

245. (New) The agent of Claim 243, wherein the antagonist is an anti-PRO224, anti-PRO9783, anti-PRO1108, anti-PRO34000, anti-PRO240, anti-PRO943, anti-hu A33, anti-PRO230, anti-PRO178, anti-PRO1199, anti-PRO4333, anti-PRO1336, anti-PRO19598, anti-

PRO1083, anti-hu TRPM2 or anti-PRO1801 antibody.

246. (New) A method of modulating the expression of a PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide, the method comprising administering to a host cell expressing said PRO224, PRO9783, PRO1108, PRO34000, PRO240, PRO943, hu A33, PRO230, PRO178, PRO1199, PRO4333, PRO1336, PRO19598, PRO1083, hu TRPM2 or PRO1801 polypeptide, an effective amount of the agent of Claim 242, thereby effectively modulating the expression of said polypeptide.